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M.L.

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

IN RE APPLICATION OF: Rastinejad et al. :  
 APPLICATION NO.: Express Mail EE645346666US : Examiner: unassigned  
 FILING DATE: November 19, 1999 : Group Art Unit: unassigned  
 TITLE: Methods and Compositions for :  
 Restoring Conformational Stability of a :  
 Protein of the p53 Family :

Hon. Assistant Commissioner for Patents  
 Washington, D.C. 20231

Sir:

Preliminary Amendment

Prior to examination herein, Applicants respectfully request entry of the following amendment.

In the Specification

As the first paragraph of the text, immediately below the "Title of the Invention" please insert the following:

-- The present application claims priority under 35 USC section 119(e) of United States Provisional Application 60/110,542, filed December 2, 1998, the complete text and figures thereof being incorporated by reference herein, as if fully set forth. --

Respectfully submitted,

*EVD*

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Dated: November 19, 1999

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species (referred to as compound "X") is depicted in Figure 2 of the Specification, and is also the subject of *in vivo* model Example 4 (pages 49-50), and Figures 5 and 6 (see also pages 11-12).

Please add the following new claims

  
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--26. (new) ~~A method of treating a human patient for cancer comprising the steps of:~~

~~(a) administering to said patient an organic non-peptide compound that binds to one or more domains of a human protein of the p53 family under physiological conditions, and stabilizes a functional conformation of said protein, and~~

~~(b) permitting said stabilized protein to interact with one or more macromolecules that participate in a wild-type activity of said protein.~~

27. (new) The method of claim 26 wherein said protein is selected from the group consisting of p53, p63 and p73.

28. (new) The method of claim 26 wherein said protein is p53.

29. (new) The method of claim 26 wherein said organic non-peptide compound binds to the DNA binding domain, residues 94-312, of human p53 protein.


30. (new) The method of claim 26 wherein the protein of the p53 family targeted by said organic non-peptide compound is wild type.

31. (new) The method of claim 26 wherein the protein of the p53 family targeted by said organic non-peptide compound is a mutant encoded by an allelic variant.

32. (new) The method of claim 26, wherein the DNA binding domain of said protein comprises a missense mutation at an amino acid position selected from the group consisting of residues 143, 173, 175, 241, and 249 of p53.

33. (new) The method of claim 26 wherein steps (a) and (b) are performed sequentially.

34. (new) The method of claim 26 wherein steps (a) and (b) are performed simultaneously.

  
35. (new) ~~The method of claim 26 wherein said cancer disease state is associated with possession of a mutant protein of the p53 family having one or more diminished wild type activities, comprising the steps of:~~

~~(a) administering to said patient an organic non-peptide compound that binds to one or more domains in said mutant protein under physiological conditions, and stabilizes a functional conformation of said protein, and~~

~~(b) permitting said stabilized protein to interact with one or macromolecules that participate in said wild type activity. --~~